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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/072,641	02/07/2002	Gregory L. Verdine	H00498/70118 TJO/TC	3255

23628 7590 06/25/2004

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EXAMINER

MCINTOSH III, TRAVISS C

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/072,641

Applicant(s)

VERDINE ET AL.

Examiner

Traviss C McIntosh

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 and 31-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 31-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>2/17/04</u> . | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1623

DETAILED ACTION

The Amendment filed February 17, 2004 has been received, entered into the record, and carefully considered. The following information provided in the amendment affects the instant application by:

Claims 2-3, 31, and 34 have been amended.

Claims 8-30, and 37-48 are canceled.

Remarks drawn to rejections of Office Action mailed August 13, 2003 include:

112 2nd paragraph rejections: which have been overcome in part by applicant's amendments and have been withdrawn in part.

102(b) rejection: which has been overcome by applicant's arguments and has been withdrawn.

103(a) rejection: which has been maintained for reasons of record.

An action on the merits of claims 1-7, and 31-36 is contained herein below. The text of those sections of Title 35, US Code which are not included in this action can be found in a prior Office action.

Information Disclosure Statement

Receipt is acknowledged of the information disclosure statement filed February 17, 2004, however, the examiner has lined through this reference as being not considered as this reference was submitted on the original IDS filed September 20, 2002 (reference 29).

Art Unit: 1623

Claim Rejections - 35 USC § 112

Claims 1-7 and 31-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection of claim 1 as being indefinite wherein the structural formula set forth in the claim has dangling valences, which leaves uncertainty as to exactly what is to be encompassed by the instant claims, is maintained for reasons of record. Applicants argue that the structure having a negative charge without reciting the balancing positive ion or other species is definite as the claim is open ended (comprising), and one of skill in the art would recognize that compositions having negatively-charged functional groups can exist and can be balanced by positively-charged ions or groups of wide variety. However, without clearly setting forth the structure of the compound to be used in the composition, one of skill in the art would not be appraised of the metes and bounds of the claim.

The rejection of claims 1-3 for being indefinite because the claims are drawn to composition claims which only comprise one ingredient is maintained for reasons of record. Claim 1 is drawn to a composition comprising a singular component, which is the compound set forth therein. Claims 2 and 3 both provide limitations to the compound set forth in claim 1. A composition cannot be comprised of a single component, as standard representation of compositions requires at least 2 components, i.e., a compound and a carrier. Applicants argue that the claims are definite composition claims as the claim is open ended, and thus the composition comprises the compound and any other agent. However, composition claims must contain at least 2 agents, as the open-ended language will not substitute for a composition when

Art Unit: 1623

there is no additional agent. That is, while the claim is open ended, and can include additional agents, it is not required, and thus when there is nothing additional added (i.e., a carrier, diluent, excipient), then the claim is read as a compound claim, as the only thing included therein is the compound represented by the structure as set forth in claim 1. Adding an additional agent for which there is support founded in the specification as originally filed to the composition claims would be seen to obviate the instant rejection.

The rejection of claim 3 as being indefinite wherein the claim reads, “wherein a hydrogen atom on a base has been substituted...” is overcome and withdrawn due to applicant’s amendments.

The rejection of claim 3 for including the term “electron-rich”, which is a relative term, as being indefinite is maintained for reasons of record. The term “electron-rich” is not defined by the claim and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Clarity is respectfully requested. Applicants argue that one of skill in the art would be appraised as to what an electron rich group is and that the specification defines what is intended. However, it is noted that in the examination process, it is proper to use the specification to interpret what applicant intends by a word or phrase recited in the claims, but it is **not** proper to read these limitations appearing in the specification into the claim when these limitations are not recited in the claim. See *In re Paulsen*, 30 F. 3d 1475, 1480, 31 USPQ2d 1671, 1674 (Fed. Cir. 1994).

The rejection of claim 4 as being indefinite wherein the claim is drawn to a method of producing a composition comprising the steps of “providing a species comprising a nucleoside,

Art Unit: 1623

and reacting the species with a compound to form a composition comprising the compound disclosed in claim 4 is withdrawn due to applicant's arguments.

The rejection of claims 6 and 7 as being indefinite wherein applicants claim a "deoxyuridine derivative" is maintained for reasons of record. In the absence of the identity of moieties intended to modify an art recognized chemical core, described structurally or by chemical name, the identity of a derivative would be difficult to ascertain. In the absence of said moieties, the claims containing the term "derivative" are not described sufficiently to distinctly point out that which applicant intends as their invention. Applicants argue that one of skill in the art would understand the meaning of derivative and that there are over 20,000 patents with claims reciting "derivatives". However, it is noted that "derivative" is not defined in the claim, and one could derivatize deoxyuridine to any of thousands of compounds, which would subsequently have divergent properties, cores, and functional groups, with enough derivatization steps. Moreover, it is well established that allowance of similar claims in another case is immaterial. See *In re Giolito*, 530, *m F.2d* 397, 188, *USPQ* 645 (CCPA 1976). Applicants are encouraged to define that which is intended by a "deoxyuridine derivative" in the claims.

The rejection of claim 31 as being indefinite wherein the claim defines R^1 and R^2 as: " R^1 and R^2 each comprising an atom, wherein at least one of R^1 and R^2 comprises a carbon atom" is maintained for reasons of record. Defining R^1 and R^2 as "comprising an atom" is not a definition which is acceptable under 112 2nd paragraph. Applicants should define every variable as to what they are intended to be, defining variables as "atoms" is not a proper definition which clearly sets for the metes and bounds of the claims.

Art Unit: 1623

The rejection of claim 34 as lacking antecedent support is obviated by applicant's amendments.

Claim 34 is indefinite wherein the claim is drawn to "a method of synthesizing a compound comprising: providing a composition and coupling a reporting group to the composition". However, it is unclear how this method would produce a compound, as applicants are adding a reporting group to a composition, which would thus form another composition, not a compound.

Claim Rejections - 35 USC § 103

The rejection of claims 1-3 under 35 U.S.C. 103(a) as being unpatentable over Engelhardt et al. (US Patent 5,241,060) is maintained for reasons of record.

Claim 1 is drawn to the composition comprising the 5-amino-2'-deoxyuridine phosphates of claim 1. Claim 2 provides the limitation of incorporating a radioactive atom onto the compound, and claim 3 provides the limitation that a hydrogen atom on the base has been substituted by an electron rich group.

Engelhardt et al. teach of a modified nucleotide which has a detectable moiety on the base (abstract). Specifically, Engelhardt teaches of 5-amino-2'-deoxyuridine biotin-labeled complexes and that it is known to produce nucleotides which are radioactively labeled to produce compounds which are useful to detect, monitor, localize, and isolate nucleic acids and other molecules of scientific or clinical interest (column 1, lines 14-20). Engelhardt et al. additionally teach to phosphorylate their nucleosides (see examples XVIII and XIX).

Art Unit: 1623

What Engelhardt et al. does not teach is compositions comprising the specific 5-amino-2'-deoxyuridine nucleoside which is phosphorylated and subsequently labeled with radioactive groups or to use electron-rich groups.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate other labels into the 5-amino-2'-deoxyuridine complex, as this is standard practice in the art. Various labels are known to be used for various purposes, and in divergent situations, divergent labels are sometimes used. It is noted that just because the preferred embodiment of Engelhardt et al. is biotin labels, that does not render unobvious the portion of the reference which teaches of the other labels, such as the radioactive labels set forth in column 1, lines 14-25.

Applicants argue that the office action does not point to a teaching, suggestion, or motivation for 5-amino-2'-deoxyuridine phosphate structures and that it is not seen why one of ordinary skill in the art would be motivated to combine examples XV, XVIII, and XIX to produce the structure claimed in claim 1. However, Engelhardt et al. teach in column 1, lines 26-30 that "it has been proposed to chemically label compounds of interest, such as **nucleotides** and **polynucleotides**". The fact that Engelhardt et al. point to nucleotides and polynucleotides as compounds of interest provides motivation to phosphorylate a nucleoside to a nucleotide, as it is known that nucleotides comprise a phosphorous moiety and the nucleosides do not. Moreover, Engelhardt et al. teach that labels can be attached to 5-amino-2'-deoxyuridine (example XV) and that 5-substituted pyrimidine nucleosides (which 5-amino-2'-deoxyuridine is) can be phosphorylated into their monophosphate and the triphosphate forms. Moreover, it is obvious to add a carrier to an obvious compound. See *Ex parte Douros*, 163 USPQ 667 (PTO Bd. App.

Art Unit: 1623

1968). 5-amino-2'-deoxyuridine phosphate compounds are obvious in view of Engelhardt, and a composition comprising the same is obvious as Engelhardt et al. teach that their compounds have utility as labeled nucleotides.

The rejection of claims 34-36 under 35 U.S.C. 103(a) as being unpatentable over Engelhardt et al. as applied to claims 1-3 above is maintained for reasons of record.

Claims 34-36 of the instant application are drawn to a method of producing a compound comprising coupling a reporting group (a radioactive or fluorescent group) to a 5-amino-2'-deoxyuridine phosphate compound.

Engelhardt et al. teach to attach a reporting group to the non-phosphate 5-amino-2'-deoxyuridine molecule, then to phosphorylate the complex (see examples). However, it has been held that merely reversing the order of steps in a multi-step process is not a patentable modification absent unexpected or unobvious results. See *Ex Parte Rubin, 128 USPQ 440 (POBA 1959)*. Applicant's arguments are set forth as correlative to the arguments for claims 1-3, and are addressed above.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

Art Unit: 1623

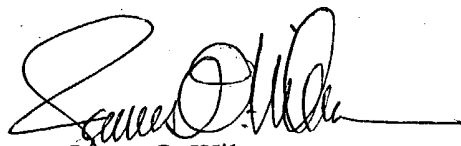
the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Traviss C. McIntosh III
June 15, 2004



James O. Wilson
Supervisory Patent Examiner
Art Unit 1623